Hepatitis C Virus: The Challenge & The Opportunity
Disclosures for Dr. Cody Chastain

- No financial disclosures
Objectives

At the end of this lecture, the learner will be able to:

- Identify important trends in hepatitis C virus (HCV) epidemiology;
- Understand the natural history of HCV;
- Describe current screening criteria for HCV and apply to clinical practice;
- Identify clinical manifestations of HCV;
- Discuss the principles of and indications for HCV treatment.
Outline

- Epidemiology and Natural History
- Clinical Manifestations
- When and Who To Treat
Outline

- Epidemiology and Natural History
- Clinical Manifestations
- When and Who To Treat
Hepatitis C Virus (HCV)

- Single-strand, positive sense RNA flavivirus
- Spread through blood and body fluids
- Predominantly infects liver cells
- No latent reservoir
  - I.e. no integration with host DNA as with HIV
  - I.e. no covalently closed DNA within host cells
  - I.e. can be eradicated/cured
HCV Epidemiology & Natural History

- Epidemiology
  - 2.3-6 million Americans infected with HCV
  - Peak rates of decompensated cirrhosis, liver cancer, and mortality estimated as 2020-2034

- Natural history
  - Minority develop advanced liver disease
  - Cirrhosis usually takes years to develop in the absence of comorbidities
  - Timeline may be accelerated by comorbidities, including alcohol use, HBV, HIV, insulin resistance, and/or obesity

Estimated HCV Ab Prevalence Rate / 100,000 persons

HepVu (www.hepvu.org). Emory University, Rollins School of Public Health.
Rate of Deaths Related to HCV per 100,000 persons

HepVu (www.hepvu.org). Emory University, Rollins School of Public Health.
HCV and Mortality in the USA

Annual number of hepatitis C-related deaths vs. other nationally notifiable infectious conditions in the US, 2003-2013

Source: Centers for Disease Control and Prevention
Figure 27 - Case Counts of Newly Reported Confirmed and Probable Chronic HCV Infection by Age and Sex, Tennessee, 2014–2018
The Opioid Epidemic and Hepatitis C in the United States

In 2017, injection drug use contributed to the nearly 48,000 opioid-related overdose deaths.

When opioids are injected, they can cause the spread of infectious diseases, like Hepatitis C.

350% Increase in New Hepatitis C Infections 2010-2016

Since 2005, new Hepatitis C infections have been rising particularly among young people, likely due to injection drug use.

Geographic areas experiencing the highest burden of opioid use disorder are also experiencing higher rates of Hepatitis C.

HepVu.org

SOURCE: U.S. Centers for Disease Control and Prevention
Areas, like Appalachia, that are heavily impacted by the opioid epidemic are experiencing high rates of Hepatitis B and C.

Kentucky, West Virginia, and Tennessee represent three of the top ten states hardest-hit by Hepatitis C.
Increases in Hepatitis C Virus Infection Related to Injection Drug Use Among Persons Aged ≤30 Years — Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012

Jon E. Zibbell, PhD1, Kashif Iqbal, MPH1, Rajiv C. Patel, MPH1, Anil Suryaprasad, MD1, Karby J. Sanders, MSN2, Loreta Moore-Moravian3, Jamie Serritella, MBA3, Steven Blankenship, MS3, John W. Ward, MD1, Deborah Holtzman, PhD1 (Author affiliations at end of text)
### Reported Cases of Acute HCV in Tennessee

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<tbody>
<tr>
<td><strong>US</strong></td>
<td>case rate</td>
<td>0.4</td>
<td>0.6</td>
<td>0.7</td>
<td>0.7</td>
<td>0.8</td>
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<tr>
<td></td>
<td>cases</td>
<td>1,229</td>
<td>1,778</td>
<td>2,138</td>
<td>2,194</td>
<td>2,436</td>
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<tr>
<td><strong>TN</strong></td>
<td>case rate</td>
<td>1.3</td>
<td>2.0</td>
<td>1.5</td>
<td>1.9</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>cases</td>
<td>83</td>
<td>129</td>
<td>98</td>
<td>123</td>
<td>173</td>
</tr>
<tr>
<td></td>
<td><strong>rank</strong></td>
<td>4th</td>
<td>4th</td>
<td>6th</td>
<td>5th</td>
<td>4th</td>
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* per 100,000 population

CASE STUDIES
Two Patients

Sam

- 25 y/o woman presents to establish care
- Past Medical History:
  - Gestational DM
  - Two SVD
- Past Surgical History
  - Appendectomy at age 12
- Past Family History
  - Adopted
- Past Social History
  - Works in cosmetics
  - Smokes tobacco
  - Drinks 2-3 drinks several times per week
  - Opioid use, including IV drug use

Chris

- 64 y/o man presents to establish care
- Past Medical History:
  - Hypertension
  - Diabetes
- Past Surgical History:
  - Tonsillectomy as a child
- Past Family History:
  - CAD, DM, lung cancer
- Past Social History:
  - Engineer
  - Denies tobacco
  - Occasional social alcohol use
  - No prior drug use
Two Patients

Sam

- **Physical:**
  - Unremarkable other than antecubital scarring and tattoos

- **Labs:**
  - CBC within normal limits other than Hgb 12
  - CMP notable for AST of 115 and ALT of 230 with a normal bilirubin and a normal albumin

Chris

- **Physical:**
  - Within normal limits though with mild hepatomegaly

- **Labs:**
  - CBC notable for WBC of 3.7 and Platelets of 115
  - CMP notable for AST of 87 and ALT of 65 with a normal bilirubin and a normal albumin
What are these patients’ indication for HCV screening as per the USPSTF?
Who is at Risk for HCV?

- Injection drug use
- Tattoo/piercing recipients
- Blood/clotting protein recipients prior to 1992
- Mother-to-child transmission from HCV+ mother
- Hemodialysis patients
- People with HIV
- Occupational exposures
- Born between 1945-1965 ("baby boomer" generation)
Who is at Risk for HCV?

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Draft Recommendation Statement

Hepatitis C Virus Infection in Adolescents and Adults: Screening

This opportunity for public comment expired on September 23, 2019 at 8:00 PM EST

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What's This?)</th>
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<tr>
<td>Adults ages 18 to 79 years</td>
<td>The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults ages 18 to 79 years.</td>
<td>B</td>
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</tbody>
</table>
Diagnostics Review

- HCV Antibody
  - Tests for *exposure*
  - Near 100% sensitivity once >6 months after infection

- HCV RNA
  - Tests for *active infection*
  - 20% or more patients spontaneously clear HCV

- HCV Genotype
  - Defines genetic subtype for prognostic information and treatment guidance

* Chronic HCV-Infected: N=3,500,000.
† Calculated as estimated number chronic HCV-infected (3,500,000) x estimated percentage diagnosed and aware of their infection (49.8%); n=1,743,000.
‡ Calculated as estimated number diagnosed and aware (1,743,000) x estimated percentage with access to outpatient care (66.9%); n=1,514,667.
§ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage HCV RNA confirmed (62.9%); n=952,726.
¶ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage who underwent liver biopsy (36.4%); n=581,632.
‖ Calculated as estimated number with access to outpatient care (1,514,667) x estimated percentage prescribed HCV treatment (36.7%); n=555,883.
** Calculated as estimated number prescribed HCV treatment (555,883) x estimated percentage who achieved SVR (58.8%); n=326,859.

Note: Only non-VA studies are included in the above HCV treatment cascade.
Sam and Chris

- Both of your patient’s HCV antibodies are positive.

- You inform the patients of their laboratory testing, and they return for evaluation.

- Sam is unconcerned about the diagnosis; she states that many her peers have HCV.

- Upon Chris’s return, he asks how long he has before he will die from liver failure…
Outline

- Epidemiology and Natural History
- Clinical Manifestations
- When and Who To Treat
Manifestations of HCV

- Acute HCV (~20%)
  - Fever
  - Fatigue and anorexia
  - Nausea and vomiting
  - Abdominal pain
  - Jaundice, dark urine, and clay-colored stools
  - Arthralgias

- Chronic HCV
  - Often asymptomatic
  - May cause fatigue, insomnia, depression, and mental status changes
  - May cause extrahepatic manifestations including vasculitis and renal disease
  - Long-term outcomes include cirrhosis, liver failure, and hepatocellular carcinoma
Sam and Chris Continued

- You counsel Sam about the potential impacts of HCV on her health over time.

- You reassure Chris that he is unlikely to imminently die of liver failure.

- They both would like to be assessed for treatment.
Outline

- Epidemiology and Natural History
- Clinical Manifestations
- When and Who To Treat
Effective Treatment Will Significantly Reduce Mortality from HCV Infection\textsuperscript{14}

![Graph showing all-cause mortality comparison between With SVR and Without SVR.]

- **All-cause mortality**
  - **P < 0.001**
  - **No. at risk**
    - With SVR: 192, 181, 168, 162, 155, 144, 125, 88, 56, 40, 28

van der Meer AJ et al. JAMA. 2012
## Goal of Treatment

<table>
<thead>
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<th>RECOMMENDED</th>
<th>RATING</th>
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<tr>
<td>The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.</td>
<td>I, A</td>
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High Priority for Treatment Owing to High Risk for Complications

- **Fibrosis (Metavir F2)**
  - Rating: Class I, level B

- **HIV-1 coinfection**
  - Rating: Class I, level A

- **Hepatitis B virus**
  - Rating: Class IIa, Level C

- **Other coexistent liver disease**
  - Rating: Class IIa, Level C

- **Debilitating fatigue**
  - Rating: Class IIa, Level C

- **Type 2 Diabetes mellitus (not diet resistant)**
  - Rating: Class IIa, Level C

- **Porphyria cutanea tarda**
  - Rating: Class IIb, Level C
<table>
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<td>Treatment is recommended for all patients with acute or chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.</td>
<td>I, A</td>
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Challenges

- Ongoing epidemic
- Effective screening
- Linkage to care
- Access to treaters
- Access to treatment
Treatment Capacity

- Providers with HCV training can deliver excellent cure rates in community practice
  - Nonrandomized open-label clinical trial
  - Included NPs, PCPs, and Specialists
  - 600 patients
  - SVR 89.3% vs. 86.9% vs. 83.8% (with specialists LOWEST)

- Uptake among non-specialist providers remains low to date
QUESTIONS?